

located in said probe such that, when said probe hybridizes to said target nucleic acid said compound is in a loop that does not participate in complementary base pairing with a nucleotide of said target nucleic acid; and

b) detecting the fluorescence produced by said fluorescent nucleotide when said probe forms a hybrid duplex with said target nucleic acid.

Please add new claims 46 and 47 as follows:

46. (New) An oligonucleotide in accordance with claim 18 wherein R⁶ and R⁷ are both adenosine.

47. (New) An oligonucleotide in accordance with claim 46 wherein an adenosine is next to R⁶ and an adenosine is next to R⁷.

REMARKS

Claims 1-4, 10-12, and 18-47 are pending in this application and presented for examination. Claims 5-9, and 13-17 have been canceled without prejudice or disclaimer. Claims 1-4, 10-12, 18-19, 22 and 29 have been amended. Claims 46-47 are newly added. No new matter has been introduced with the forgoing amendments and newly added claims.

Attached hereto is a marked-up version of the changes made to the specification and claims by the current amendment. The attached page is captioned "Version with markings to show changes made." Early examination is respectfully requested.

I. FORMALITIES

Support for the addition of "at least one of R⁶ and R⁷ is a phosphate covalently attached to adenosine" in claims 18 and 29, and of R⁷ being a phosphate "covalently attached to adenosine" in claims 19 and 22, is supported by sequence ID Nos. 1, 2, 7, 9, 10, 11, 12, 19, 21 and 22.

Support for new claims 46-47 is found throughout the application as filed. More particularly, support is found, for example, in sequence IDs 10 and 22 in Table 2.

As such, no new matter has been introduced and Applicants respectfully request they be entered.

The Examiner has indicated that restriction to one of the following inventions is required under 35 U.S.C. § 121:

Group I. Claims 1-17, drawn to a compound.

Group II. Claims 18-45, drawn to an oligonucleotide and method of use.

In response, Applicants hereby elect Group II, drawn to an oligonucleotide and method of use, with traverse. Claims readable thereon include claims 18-45 and new claims 46 and 47.

In response to the election of species requirement, Applicants elect the following species:

SEQ ID 10.

Applicants assert that the Examiner has improperly used restriction practice in this present 371 national phase application.

Under MPEP § 1893(d), When making a lack of unity of invention requirement, the examiner must (1) list the different groups of claims and (2) explain why each group lacks unity with each other group (i.e., *why* there is no single general inventive concept) **specifically describing the unique special technical feature in each group.**
[Emphasis added]

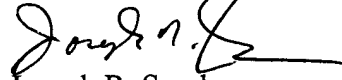
In the instant case, the Examiner has failed to describe the unique technical feature in each group, but instead reverts to restriction practice parlance stating that "Group I can be used in materially different process...".

Moreover, the issue of unity of invention was already decided during Chapter I of the International Application.

As such, Applicants respectfully request that the Examiner join the two groups, or alternatively, specifically describe the unique special technical feature in each group.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 925-472-5000.

Respectfully submitted,

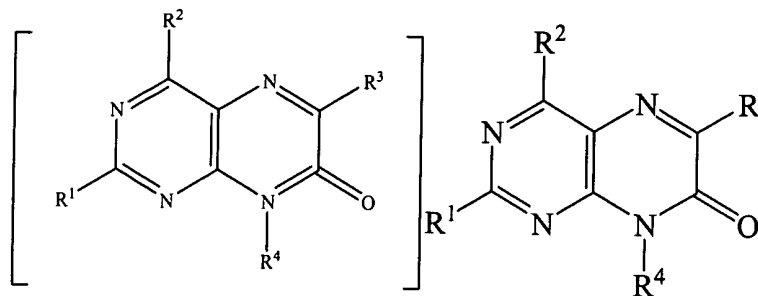


Joseph R. Snyder
Reg. No. 39,381

TOWNSEND and TOWNSEND and CREW LLP
Two Embarcadero Center, 8th Floor
San Francisco, California 94111-3834
Tel: (415) 576-0200
Fax: (415) 576-0300
JS:dad

VERSION WITH MARKINGS TO SHOW CHANGES MADE

1. (Amended) A compound of the formula:



wherein:

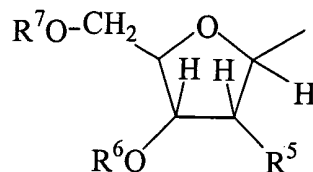
R¹ is a member selected from the group consisting of hydrogen and optionally substituted C₁-C₆-alkyl;

R² is a member selected from the group consisting of amino and mono- or di-substituted amino wherein the substituent is a protecting group;

R³ is optionally substituted C₁-C₆ alkyl;

R⁴ is [a member selected from the group consisting of hydrogen and]L;

L is of the formula



wherein:

R⁵ is [a member selected from the group consisting of hydrogen,]hydroxyl[, and substituted hydroxyl wherein the substituent is a protecting group]; R⁶ is a member selected from the group consisting of hydrogen, phosphoramidite, an H-phosphonate, a methyl phosphonate, a phosphorothioate, a phosphotriester, a hemisuccinate, a hemisuccinate covalently bound to a solid support, a dicyclohexylcarbodiimide, and a dicyclohexylcarbodiimide covalently bound to a solid support, a hydroxyalkyl, and a hydroxyalkyl covalently bound to a solid support; and

R⁷ is a member selected from the group consisting of hydrogen, a phosphate, a triphosphate, and a protecting group[;

with the proviso that R^1 and R^4 are not simultaneously L].

2. (Amended) A compound in accordance with claim Error! Reference source not found., wherein R^1 is hydrogen;

R^2 is a member selected from the group consisting of amino, mono-, and di-substituted amino wherein the substituents are members selected from the group consisting of benzoyl, isobutyryl, phthaloyl, di-n-butylaminomethylidene, dimethylaminomethylidene, p-nitrophenylethoxycarbonyl and dimethylaminomethylenamino;

R^4 is L;

R^5 is [a member selected from the group consisting of hydrogen,]hydroxyl[, hydroxyl substituted with a member selected from the group consisting of trityl, monomethoxytrityl, dimethoxytrityl, tetrahydropyran-1-yl, 4-methoxytetrahydropyran-4-yl, 1-(2-chloro-4-methyl)phenyl-4-methoxypiperidin-4-yl, t-butyldimethylsilyl, p-nitrophenylethylsulfonyl, tetrahydropyranyl, 4-methoxytetrahydropyranyl, 2-nitrobenzyl, 9-phenylxanthen-9-yl and p-nitrophenylethyl];

R^6 is a member selected from the group consisting of consisting of hydrogen, phosphoramidite, H-phosphonate, hemisuccinate, and hemisuccinate covalently bound to a solid support; and

R^7 is a member selected from the group consisting of hydrogen, trityl, monomethoxytrityl, dimethoxytrityl, phthaloyl, di-n-butylaminomethylene, dimethylaminomethylidene and triphosphate.

3. (Amended) A compound in accordance with claim Error! Reference source not found., wherein R^2 is a member selected from the group consisting of amino and an amino group mono-substituted by a protecting group selected from the group consisting of di-n-butylaminomethylidene, p-nitrophenylethoxycarbonyl, and dimethylaminomethylenamino;

R^5 is [a member selected from the group consisting of hydrogen,]hydroxyl[, and hydroxyl substituted with a member selected from the group consisting of dimethoxytrityl, tetrahydropyran-1-yl, t-butyldimethylsilyl, 2-nitrobenzyl, and p-nitrophenylethylsulfonyl];

R^6 is a member selected from the group consisting of hydrogen, β -cyanoethyl-N-diisopropyl phosphoramidite and a hemisuccinate covalently bound to controlled pore glass; and

R^7 is a member selected from the group consisting of dimethoxytrityl, di-n-butylaminomethylene, and dimethylaminomethylidene.

4. (Amended) A compound in accordance with claim Error! Reference source not found., wherein R^2 is a member selected from the group consisting of amino and an amino group mono-substituted by a protecting group selected from the group consisting of di-n-butylaminomethylidene, p-nitrophenylethoxycarbonyl, and dimethylaminomethylenamino;

R^5 is [a member selected from the group consisting of hydrogen and]hydroxyl[substituted with a member selected from the group consisting of dimethoxytrityl, tetrahydropyran-1-yl, t-butyldimethylsilyl, 2-nitrobenzyl, and p-nitrophenylethyl];

R^6 is a member selected from the group consisting of hydrogen and β -cyanoethyl-N-diisopropyl phosphoramidite; and

R^7 is a member selected from the group consisting of hydrogen and dimethoxytrityl.

5. (Canceled)

6. (Canceled)

7. (Canceled)

8. (Canceled)

9. (Canceled)

10. (Amended) A compound in accordance with claim Error! Reference source not found., wherein;

R^1 is optionally substituted C_1 - C_6 alkyl;

R^2 is a member selected from the group consisting of amino, mono-, and di-substituted amino wherein the substituent is a member selected from the group consisting of benzoyl, isobutyryl, phthaloyl, di-n-butylaminomethylidene, dimethylaminomethylidene, p-nitrophenylethoxycarbonyl and dimethylaminomethylenamino;

R^3 is optionally substituted C_1 - C_6 alkyl;

R^4 is L;

R^5 is [a member selected from the group consisting of hydrogen,]hydroxyl[and hydroxyl substituted with a member selected from the group consisting of trityl, monomethoxytrityl, dimethoxytrityl, tetrahydropyran-1-yl, 4-methoxytetrahydropyran-4-yl, 1-(2-chloro-4-methyl)phenyl-4-methoxypiperidin-4-yl, t-butyldimethylsilyl, p-nitrophenylethylsulfonyl, tetrahydropyranyl, 4-methoxytetrahydropyranyl, 2-nitrobenzyl, 9-phenylxanthen-9-yl and p-nitrophenylethyl];

R^6 is a member selected from the group consisting of hydrogen, H-phosphonate, phosphoramidite, hemisuccinate, and hemisuccinate covalently bound to a solid support; and

R^7 is a member selected from the group consisting of hydrogen, trityl, monomethoxytrityl, dimethoxytrityl, phthaloyl, di-n-butylaminomethylene, and dimethylaminomethylidene.

11. (Amended) A compound in accordance with claim Error! Reference source not found., wherein R^1 is methyl;

R^2 is a member selected from the group consisting of amino and an amino group mono-substituted by a protecting group selected from the group consisting of di-n-butylaminomethylidene, p-nitrophenylethoxycarbonyl, and dimethylaminomethylenamino;

R^3 is methyl;

R^5 is [a member selected from the group consisting of hydrogen,]hydroxyl[and hydroxyl substituted with a member selected from the group consisting of dimethoxytrityl, tetrahydropyran-1-yl, t-butyldimethylsilyl, 2-nitrobenzyl, and p-nitrophenylethylsulfonyl];

R^6 is a member selected from the group consisting of hydrogen, β -cyanoethyl-N-diisopropyl phosphoramidite and a hemisuccinate covalently bound to controlled pore glass; and

R^7 is a member selected from the group consisting of dimethoxytrityl, di-n-butylaminomethylene, and dimethylaminomethylidene.

12. (Amended) A compound in accordance claim Error! Reference source not found., wherein R^1 is methyl; R^2 is a member selected from the group consisting of amino and an amino group mono-substituted by a protecting group selected from the group consisting of di-n-butylaminomethylidene, p-nitrophenylethoxycarbonyl, and dimethylaminomethylenamino;

R^5 is [a member selected from the group consisting of hydrogen and hydroxyl] substituted with a member selected from the group consisting of dimethoxytrityl, tetrahydropyran-1-yl, t-butyldimethylsilyl, 2-nitrobenzyl, and p-nitrophenylethylsulfonyl];

R^6 is a member selected from the group consisting of consisting of hydrogen and β -cyanoethyl-N-diisopropyl phosphoramidite; and

R^7 is a member selected from the group consisting of hydrogen and dimethoxytrityl.

13. (Canceled)

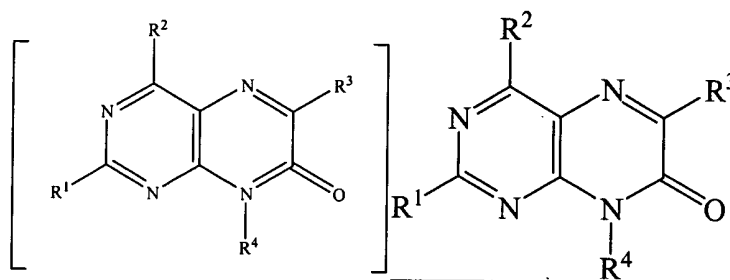
14. (Canceled)

15. (Canceled)

16. (Canceled)

17. (Canceled)

18. (Amended) An oligonucleotide comprising one or more nucleotide monomers, said monomers having the formula



wherein:

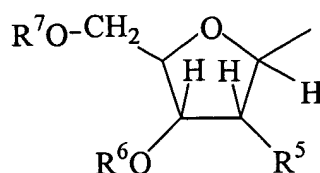
R^1 is a member selected from the group consisting of hydrogen and optionally substituted C_1 - C_6 -alkyl;

R^2 is a member selected from the group consisting of amino and mono- or di-substituted amino wherein the substituent is a protecting group;

R^3 is optional substituted C_1 - C_6 alkyl;

R^4 is L;

L is of the formula



wherein:

R^5 is a member selected from the group consisting of hydrogen and hydroxyl;

R^6 is a member selected from the group consisting of hydrogen, a phosphate, a phosphate covalently attached to a nucleotide, a phosphate covalently attached to a nucleoside; a hemisuccinate covalently bound to a solid support, a dicyclohexylcarbodiimide covalently bound to a solid support, and a hydroxyalkyl covalently bound to a solid support; and

R^7 is a member selected from the group consisting of hydrogen, a phosphate, a phosphate covalently attached to a nucleotide and a phosphate covalently attached to a nucleoside;

[with the proviso that R^1 and R^4 are not simultaneously L.]

wherein at least one of R^6 and R^7 is a phosphate covalently attached to adenosine.

19. (Amended) An oligonucleotide in accordance with claim Error!

Reference source not found., wherein:

R^1 is hydrogen;

R^2 is amino;

R^3 is methyl;

R^5 is hydrogen and hydroxyl;

R^6 is hydrogen; and

R^7 is a phosphate covalently attached to adenosine.

22. (Amended) An oligonucleotide in accordance with claim Error!

Reference source not found., wherein:

R^1 is optionally substituted C_1 - C_6 -alkyl;

R^2 is amino;

R^3 is methyl;

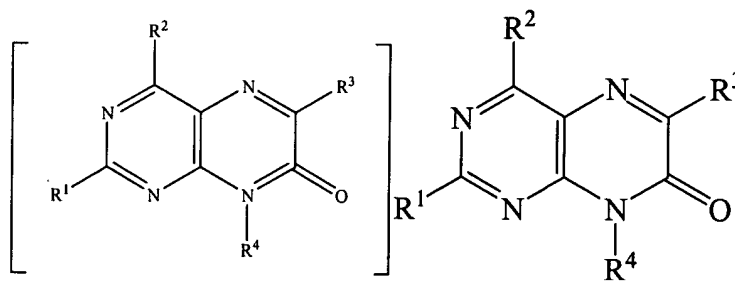
R^5 is hydrogen and hydroxyl;

R^6 is hydrogen; and

R^7 is a phosphate covalently attached to adenosine.

29. (Amended) A method of detecting the presence, absence, or quantity of a target nucleic acid, said method comprising the steps of:

a) contacting said target nucleic acid with a nucleic acid probe wherein said nucleic acid probe comprises compound of the formula:



wherein:

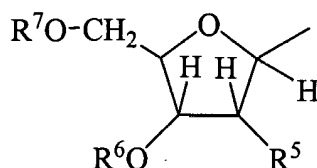
R^1 is a member selected from the group consisting of hydrogen and optionally substituted C_1 - C_6 -alkyl;

R^2 is a member selected from the group consisting of amino and mono- or di-substituted amino wherein the substituent is a protecting group;

R^3 is optionally substituted C_1 - C_6 alkyl;

R^4 is L;

L is of the formula



wherein:

R^5 is a member selected from the group consisting of hydrogen and hydroxyl;

R^6 is a member selected from the group consisting of hydrogen, phosphoramidite, an H-phosphonate, a methyl phosphonate, a phosphorothioate, a phosphotriester, a hemisuccinate, a hemisuccinate covalently bound to a solid support, a dicyclohexylcarbodiimide, and a dicyclohexylcarbodiimide covalently bound to a solid support; and

R^7 is a member selected from the group consisting of a phosphate covalently attached to a nucleotide and a phosphate covalently attached to a nucleoside;

[with the proviso that R^1 and R^4 are not simultaneously L;]

wherein, at least one of R^6 and R^7 is a phosphate covalently attached to adenosine;

located in said probe such that, when said probe hybridizes to said target nucleic acid said compound is in a loop that does not participate in complementary base pairing with a nucleotide of said target nucleic acid; and

b) detecting the fluorescence produced by said fluorescent nucleotide when said probe forms a hybrid duplex with said target nucleic acid.

46. (New) An oligonucleotide in accordance with claim 18 wherein R^6 and R^7 are both adenosine.

47. (New) An oligonucleotide in accordance with claim 46 wherein an adenosine is next to R^6 and an adenosine is next to R^7 .